

A Correlation between Leptin and Thyroid Hormones in Population with Obesity

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ABSTRACT

Background: Obesity has become a major problem in Southeast Asian countries, including Indonesia. Adipocyte cells produce leptin, which plays a role in regulating one's appetite and is associated with obesity. In obesity, chronic inflammation occurs, altering various hormonal activities throughout the body, including the activities of thyroid hormones. However, the correlation between leptin levels and thyroid hormone levels in obese population remains unclear.

Aim: To determine the correlation between leptin levels and thyroid hormone levels in obese population.

Method. This study involved 33 participants with obesity (BMI >27) at Diponegoro National Hospital, Semarang. Leptin levels were measured using enzyme-linked immunoassay (ELISA), while thyroid hormones (TSH, T3, FT3, T4 and FT4) were measured using immunology analyzer. Correlation analyses between variables were performed using Pearson and Spearman correlation test.

Results: There was a significant positive correlation between leptin levels and TSH level ($r=0.503$; $p=0.003$). There were no correlations between leptin levels and levels of T3, FT3, T4 and FT4.

Conclusion: Leptin levels might influence TSH levels, and both leptin and thyroid hormones might impact on therapeutic approach in patients with obesity.

Keywords: leptin, thyroid hormones, TSH, obesity

INTRODUCTION

Obesity has become a major problem in Southeast Asian countries, including Indonesia. The prevalence of overweight and obesity in World Health Organization (WHO) members in Southeast Asian countries has increased up to 8–30% in men and 8–52% in women.⁽¹⁾ The prevalence of adult obese male population in 2013 was 19.7 percent, which was higher than in 2007 (13.9%) and in 2010 (7.8%), while the prevalence of adult obese women (>18 years) has increased to 32.9% in 2013, showing an increase of 18.1% from 2007 (13.9%) and 17.5% from 2010 (15.5%).⁽²⁾

Obesity is defined as a condition with an increase in body mass index (BMI) exceeding normal values, with BMI higher than 27,⁽²⁾ while WHO defines obesity as BMI higher than 30.^(3, 4) The causes of obesity are multifactorial, ranging from diet, physical activity, genetics, environmental factors and so forth.⁽⁵⁾

Leptin is a peptide consisting of 167 amino acids, and plays a role in regulating a person's appetite. Leptin is produced by adipocyte cells and is thought to be associated with obesity. Leptin levels seem to increase in a person with large amounts of adipocyte cells, such as in patients with obesity who have excess fat accumulation.⁽⁶⁻¹¹⁾

Obesity is also able to alter various hormonal activities in the body, including thyroid hormones. Chronic

inflammatory conditions in obese patients may cause alteration in thyroid hormones. Studies suggested that levels of thyroid stimulating hormone (TSH), free T3 (FT3), and free T4 (FT4) varied significantly between obese and control non-obese populations.⁽¹²⁻¹⁴⁾ They showed that levels of TSH increased in accordance with increasing BMI.^(14, 15)

It was suggested that there were an increase in leptin levels and an alteration in thyroid hormone in obesity which encouraged researchers to determine whether there was correlation between leptin levels and thyroid hormone levels in obese population.

METHOD

This was an observational analytic study with cross-sectional design carried out at Diponegoro National Hospital Semarang on March – October 2018. There were 33 obese participants involved in this study by consecutive sampling. Inclusion criteria were obese people in age range of 20 – 65 years with BMI>27 and normal body temperature. Patients with history of thyroid diseases, heart disease, stroke, autoimmune disease were excluded from this study.

Data consisting of patients' age, sex, weight, and height were collected in the out-patient clinic of Diponegoro National Hospital. Waist circumference was measured as a circumference located between the iliac crista and arcus

costa. It was measured by two blinded clinicians with a measuring tape in an upright position and with precision of 1 mm at expiration. Weight and height were measured with a calibrated weight scale and meter.

Subjects had their blood drawn as many as 6 cc of blood using a plain tube. All blood samples were centrifuged to obtain the serum used for leptin and thyroid profile examination consisting of TSH, T3, FT3, T4 and FT4. Leptin levels were measured in Laboratory of Faculty of Medicine, Diponegoro University Semarang. Leptin levels were measured with the ELISA principle (LEPTIN ELISA, Diagnostic Biochem Canada (DBC), Ontario, Canada) by the ELX 800 Universal Microplate reader spectrophotometer.

Thyroid hormone profiles were measured based on the Enzyme-Linked Fluorescent Assay (ELFA) principle by a compact multiparametric immunoanalyzer (MINI VIDAS® compact multiparametric immunoanalyzer, Biomerieux clinical diagnostic, Marcy-l'Etoile, France) in the laboratory of Diponegoro National Hospital Semarang. These measurements were automated quantitative test using VIDAS®FT3, VIDAS®T3, VIDAS®T4, and VIDAS®TSH.

VIDAS®FT3/VIDAS®T3/VIDAS®T4/VIDAS®TSH were from Biomerieux SA, Marcy-l'Etoile, France.

Ethical clearance has been obtained from the Ethics Commission on Health Research, Faculty of Medicine, Diponegoro University / Dr. Kariadi Hospital, Semarang. All study subjects were providing written informed consent.

RESULTS

A total of 57 subjects were involved in the study, and only 33 subjects met the criteria. The study subjects consisted of 18 (54.5%) women and 15 (45.5%) men. Baseline characteristics of the study subject are described in table 1.

The characteristics of the subjects according to gender are described in table 2.

Table 3 shows the normal leptin levels in 2 female subjects (6.1% of all study subjects) and hyperleptinemia in 16 female subjects (48.4%). All 15 male subjects (45.5%) were hyperleptinemia. In overall, there were only 2 subjects (6.1%) that had leptin levels in the range of reference values, while the remaining 31(93.9%) were hyperleptinemia.

The levels of thyroid hormones in all subjects is presented in table 4. While the correlation of leptin with thyroid hormones (TSH, T3, FT3, T4 and FT4) is presented in table 5. Our study could reveal a positive correlation between leptin and TSH ($r=0.503$; $p=0.003$). Conversely, there were no significant correlations between leptin and other thyroid hormones, namely T3, FT3, T4 and FT4 (table 5).

Table 1: Baseline characteristics in all subjects

Parameter	Mean ± SD	Median (Min-max)
Age (years)	25.5 ± 8.06	20 (18 – 46)
Waist circumference (cm)	97.1 ± 9.62	98.5 (79.5 – 116.0)
Pelvic circumference (cm)	108.8 ± 8.50	107 (88 – 126)
Height (cm)	162.6 ± 7.32	161.2 (149.0 – 175.5)
Weight (cm)	85.9 ± 13.21	87.8 (65.5 – 111.0)
BMI (kg/m ²)	32.4 ± 3.78	31.6 (27.3 – 41.6)
Leptin	43.3 ± 21.30	44.7 (14.78 – 95.72)
Level of thyroid hormone		
TSH (µIU/mL)	1.8 ± 0.94	1.6 (0.49 – 4.26)
T3	1.5 ± 0.30	1.5 (0.86 – 2.52)
FT3 (pmol/mL)	4.6 ± 0.58	4.6 (3.26 – 5.88)
T4	89.8 ± 12.1	90.1 (71.22 – 124.03)
FT4 (pmol/mL)	16.5 ± 2.38	16.5 (10.56 – 20.99)

Table 2. Subjects' characteristics according to gender

Parameter	Mean ± SD	Female	Mean ± SD	Male
		Median (min – max)		Median (Min, max)
Age (years)	26.5 ± 8.98	20 (18 – 46)	24.4 ± 6.98	20 (18 – 39)
Waist circumference (cm)	92.9 ± 8.95	91 (79.5 – 110.0)	102.0 ± 8.11	104 (89 – 116)
Pelvic circumference (cm)	108.3 ± 9.60	107 (88 – 126)	109.5 ± 7.33	107 (100 – 122)
Height (cm)	158.1 ± 4.67	158 (149 – 169)	167.7 ± 6.42	168 (157.5 – 175.5)
Weight (cm)	81.0 ± 12.25	75.9 (65.5 – 109.4)	91.5 ± 12.31	89.1 (73.8 – 111.0)
BMI (kg/m ²)	32.4 ± 4.29	31.1 (27.3 – 41.6)	32.4 ± 3.26	31.7 (28.3 – 39.3)
Leptin	52.1 ± 21.69	54.1 (17.26 – 95.72)	33.4 ± 16.39	28.1 (14.78 – 65.43)
Level of thyroid hormone				
TSH (µIU / mL)	1.8 ± 0.96	1.7 (0.49 – 4.17)	1.8 ± 0.96	1.5 (0.61 – 4.26)
T3	1.4 ± 0.25	1.4 (0.86 – 1.87)	1.6 ± 0.31	1.6 (1.13 – 2.52)
FT3 (pmol / mL)	4.4 ± 0.37	4.6 (3.77 – 5.00)	4.8 ± 0.70	4.8 (3.26 – 5.88)
T4	89.6 ± 13.30	90.4 (71.22 – 124.03)	90.1 ± 11.12	89.7 (74.92 – 107.62)
FT4 (pmol / mL)	16.5 ± 2.52	16.6 (10.88 – 20.99)	16.4 ± 2.31	17.0 (10.56 – 19.59)

Table 3. Leptin Levels according to Gender in all Study Subjects

	Age (years)	Reference value (ng/dL)	Total (n=33)	Total (n=33)
Women	<20	20.1 ± 1.24 Normal	0 (0%)	18 (54.5%)
		Hyperleptinemia	4 (12.1%)	
	20–29	19.2 ± 0.61 Normal	2 (6.1%)	
		Hyperleptinemia	5 (15.1%)	
	30–39	17.5 ± 0.55 Normal	0 (0%)	
		Hyperleptinemia	6 (18.2%)	
	40–49	20.2 ± 0.54 Normal	0 (0%)	
		Hyperleptinemia	1 (3.0%)	

Men	<20	2.9 ± 0.57 Normal	0 (0%)	15 (45.5%)
		Hyperleptinemia	3 (9.1%)	
	20–29	4.1 ± 0.26 Normal	0 (0%)	
		Hyperleptinemia	7 (21.2%)	
	30–39	5.9 ± 0.29 Normal	0 (0%)	
		Hyperleptinemia	5 (15.1%)	
Total				33 (100%)

Table 4: Thyroid Hormones Levels in all Subjects

Variable	Total
TSH	High 0 (0%)
	Normal 33 (100%)
	Low 0 (0%)
T3	High 0 (0%)
	Normal 33 (93.9%)
	Low 2 (6.1%)
FT3	High 0 (0%)
	Normal 33 (100%)
	Low 0 (0%)
T4	High 0 (0%)
	Normal 33 (100%)
	Low 0 (0%)
FT4	High 0 (0%)
	Normal 33 (100%)
	Low 0 (0%)

Table 4: Correlation between leptin and thyroid hormones

Parameters	Leptin	
TSH	0.503	0.003 * a
T3	-0.108	0.549 b
FT3	-0.017	0.923 b
T4	-0.038	0.834 b
FT4	-0.038	0.835 b

*p<0.05 was considered as statistically significant

^aSpearman correlation test

^bPearson correlation test

DISCUSSION

In our study, we found that the levels of leptin in women was higher than in men (52.1 ± 21.69ng/dL vs 33.4 ± 16.39 ng/dL, respectively). Our finding was consistent with previous studies by Hellstrom L et al that suggested significant differences in serum leptin levels between men and women, with a higher leptin levels in women compared to men. Similar results were also found in studies by Gijon-Conde T et al and Najam SS et al in which both suggested higher levels of leptin in women compared to men^{16,17,18}.

In overall, the mean leptin levels in our study subjects was 43.3 ± 21.30 ng/dL. Our finding was supported by the study of Stylianou C et al suggesting a mean leptin level in obese young adults of 46.3 ± 28.02 ng/dL.⁽¹⁹⁾ The mean leptin level in our study was lower than the mean leptin level in the study by Kazmi A et al, which was 52.8±24.6 ng/mL²⁰. The median of leptin levels in our study was 44.7 (14.78 – 95.72) ng/mL that was similar to that of previous study by van Zyl S et al with median of 44.1 (31.8 – 75.7) and with similar characteristics of study subjects²¹.

Thyroid hormone levels of TSH, T4, FT4 and FT3 in our study subjects were within the range of reference values, while 2 (6.1%) subjects showed that the levels of T3 was less than reference value. Our finding corresponded to previous study by Özer S et al which showed that there were no significant differences in TSH

levels in several criteria for obesity²².

In overall, the mean TSH levels in our study was 1.8 ± 0.94 µIU/mL; that corresponded to previous studies by Kitahara CM et al that showed an average TSH level in obesity of 1.69 µIU/mL and by Solanki A et al that of 2.64 µIU/L. Both studies by Solanki A et al and Kitahara CM et al also stated that the higher the BMI, the higher TSH levels^{15,23}.

The mean FT4 level in our study was 16.5 ± 2.38 pmol/mL that was higher than the previous studies by Alzubaidy GHH et al which was 10.3 ± 4.5 pmol/mL and by Kitahara CM et al which was 0.76 ng/dL (9.78 pmol/L)^{15,23,24,25}. The mean FT3 level in our study (4.6 ± 0.58 pmol/mL) was considerably similar to studies by Alzubaidy GHH et al which was 4.19 ± 1.38 pmol/mL and by Kitahara which was 3.21pg/mL (4.93 pmol/L)^{15,23,24,25}. It seemed that thyroid hormone levels in obese patients might vary in appearance, i.e. normal, increase, or decrease, with respect to different examination times, degrees of obesity and different types of obesity and their relation to insulin sensitivity²⁴.

Our study could reveal a positive correlation between leptin and TSH. This was similar to a study by Alzubaidy GHH et al that showed a significant correlation between leptin and TSH (r=0.79; p=0.01). Meanwhile, our study failed to show significant correlations between leptin and other thyroid hormones, namely T3, FT3, T4 and FT4. Our findings were difference to study by Alzubaidy GHH et al that showed significant negative correlations between leptin and T3 (r=-0.172; p=0.05) and also T4 (r=-0.086; p=0.05)²⁵.

These differences might occur because both studies were carried out in different populations; in which the previous study was carried out in patients with type 2 diabetes, while our study was conducted in obese young adults, regardless of glucose status²⁵.

Study by Shahramian I et al showed that there were no correlations between leptin and T3 or TSH in the pediatric population, but there was a correlation between leptin and T4²⁶. Another study by Ibrahim et al showed that there were no significant associations between leptin with thyroid hormones²⁷.

Fat cells produce leptin and alter active endocrine organs. It was suggested that the relationship between BMI and TSH was mediated by leptin produced by adipocyte tissue. Leptin physiologically regulates energy homeostasis by sending signals of fat reservation in adipose tissue to the central nervous system. This might modulate the neuroendocrine response and behavior for overfeeding, thereby regulating food intake and energy expenditure. Leptin is also an important neuroendocrine regulator of the hypothalamic-pituitary-thyroid axis, stimulation central transcription of pro thyrotropin-releasing hormone (TRH)^{24,28}. However, it was also suggested that leptin was not widely used in normal thyroid function. This might be the reason for the absence of a significant relationship

between levels of leptin and thyroid hormones, namely T3, FT3, T4 and FT4 in our study.⁽⁶⁾ Leptin also affects thyroid de-iodination activity by activating T4 to T3 conversion. All patients have hyperleptinemia, but not yet affect the thyroid gland secretion.

CONCLUSION

There was a significant positive correlation between leptin levels and TSH, however there were no correlations between leptin levels and T3, FT3, T4 and FT4. There might be hyperleptinemia in obese patients which was related to TSH levels and affected the secretion of the thyroid gland. Both leptin and thyroid hormones might impact on therapeutic approach in patients with obesity.

Conflict of interest: There was not conflict of interest in this study.

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